

# Determination of equation for estimating continuous positive airway pressure in patients with obstructive sleep apnea for the Indian population

Latha Sarma, Nandan Putti, Kapil Alias, Mohit Chilana

Department of Pulmonology, KIMS Hospital, Secunderabad, Telangana, India

## ABSTRACT

**Background:** Continuous positive airway pressure (CPAP) is the treatment of obstructive sleep apnea (OSA). The CPAP pressure is generally estimated by manual titration or an auto CPAP device. An alternative method involves the use of the predictive equation. **Aim and Objective:** There is no equation developed, taking into account the Indian population. The aim is to develop a predictive equation for optimal CPAP pressure in patients with OSA and to validate the equation by comparing it with manual titration pressure. **Materials and Methods:** A total of 250 patients with OSAS who underwent successful manual titration for CPAP treatment in a tertiary care center were included in this study and divided randomly into two groups A and B with 150 and 100 patients, respectively. Stepwise multiple regression analysis was applied to anthropometric and polysomnographic variables of group A and the predictive equation for estimating CPAP was developed using SPSS. This equation was validated by comparing the estimated pressure with that of manual titration pressure in Group B. **Results:** The mean age was  $55.09 \pm 11.43$  and mean body mass index (BMI) was  $33.69 \pm 6.56$ . CPAP pressure in patients with OSA was  $11.13 \pm 1.83$  cm H<sub>2</sub>O. The Apnea Hypopnea index (AHI) ( $r = 0.595$ ,  $P < 0.001$ ), minimal; SpO<sub>2</sub> ( $r = -0.502$ ,  $P < 0.001$ ), BMI ( $r = 0.494$ ,  $P < 0.001$ ) significantly correlated with optimal CPAP level. A predictive equation for optimal CPAP level in patients with OSA was developed using AHI, BMI, and minimal SpO<sub>2</sub>, which can be easily measured during the diagnostic process. Optimal CPAP level (cm H<sub>2</sub>O) =  $8.401 + (0.053 \times \text{BMI}) + (0.020 \times \text{AHI}) - (0.031 \times \text{lowest oxygen})$ . Twenty-six percent of the variance in the optimal CPAP level was explained by this equation ( $R^2 = 0.26$ ,  $P < 0.001$ ) and the equation showed 86% of optimal estimation. **Conclusion:** The results suggest that manual titration pressure correlates with the pressure derived from the predictive equation in our study.

**KEY WORDS:** Continuous positive airway pressure, Indian population, obstructive sleep apnea, predictive equation

**Address for correspondence:** Dr. Latha Sarma, KIMS Hospital, Secunderabad, Telangana, India. E-mail: dr.lathasarma@gmail.com

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## INTRODUCTION

The incidence of obstructive sleep apnea (OSA) is increasing in India, and men are commonly affected than women with a prevalence of 2.4%–4.96% in men and 1%–2% in women.<sup>[1]</sup> The nonsurgical and nonpharmacological treatment options available for OSA

are automatic positive airway pressure (APAP), bi-level positive airway pressure, continuous positive airway pressure (CPAP). Split night polysomnography (PSG) is performed by a technician in the center to diagnose and

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estimate the optimum airway pressure required by the patient. In the first half of the study severity of the OSA is estimated, and in the second half, the amount of airway pressure by manual titration is estimated for nullifying the apneic episodes. Few patients find it difficult in getting early sleep, and this results in the delay of the split night PSG, and the manual titration cannot be completed requiring revisits. This is usually associated with the increase in healthcare expenses to the patients. In a few centers, there is no proper equipment available for estimating titration the airway pressure.

To find alternatives in the estimation of the airway pressure, researchers have used multiple linear regressions analyses on variables such as age, apnea-hypopnea index (AHI), apnea index, body mass index (BMI), craniofacial/cephalometric features, height, lowest oxygen saturation, mean oxygen saturation, neck circumference (NC), oropharyngeal soft tissues, oxygen desaturation index (ODI), race, respiratory disturbance index (RDI), sex (male vs. female), sleepiness, smoking, and weight. The equations have subsequently been used either for estimating starting pressures or for use during in-lab PAP titration studies.<sup>[2]</sup>

Hoffstein *et al.*<sup>[3]</sup> developed and validated a formula to predict optimal CPAP settings. This equation is widely applicable for the white population, and it does not consider race or lifestyle factors that are known to affect the severity of OSA.<sup>[4]</sup> Lee *et al.* estimated and validated the equation in Korean subjects with limited usefulness in some clinical settings.<sup>[5]</sup>

There is no equation developed, taking into account the Indian population. Our study was aimed to develop a predictive equation for optimal CPAP pressure in patients with OSA and validate the equation by comparing it with manual titration pressure.

## MATERIALS AND METHODS

A retrospective observational cross-sectional study was carried out in the Department of Pulmonology of a 1000-bedded tertiary-care hospital to develop an equation for estimating pressure for the therapy. This study was conducted 6 months after taking permission from the Institutional Ethics Committee. Patient data were collected prospectively from the PSG reports given to patients in OPD after taking consent.

Selection criteria followed during inclusion were patients diagnosed with mild, or moderate, or severe OSA by either whole-night or split-night PSG within an age group of 18–80 years. Pregnant women and inconclusive sleep study patients were not included in the study.

The type of sleep study performed was split-night or whole night PSG, with 55 channel ALICE-5 PSG.

With the estimated proportion of incidence of OSA being 14%, confidence interval of 95%, power of 85%, the sample size was calculated as 250. The study population was divided randomly into two groups A and B, with 150 and 100 patients, respectively.

The variables included three anthropometric parameters (age, sex, BMI), 9 polysomnographic parameters (sleep latency, sleep efficiency, sleep state [N1, N2, N3, REM, and total]), AHI, minimal SpO<sub>2</sub>. In Group 1, we used the Pearson correlation test to evaluate the association of these variables with titrated CPAP level. Variables with *P* values. 05 in the univariate analysis were entered into a stepwise multiple linear regression analysis to identify independent predictive variables and to develop a predictive formula for optimal CPAP. In Group 2, we compared the regression equation derived from Group 1 with the manual titration pressure by the use of the Pearson correlation. The prediction was classified as optimal estimation (difference of measured pressure and predicted pressure of 1 cm H<sub>2</sub>O or less), underestimation (1 cm H<sub>2</sub>O low), or overestimation (1 cm H<sub>2</sub>O high).

## RESULTS

The number of men and women in Group 1 was 109/41 and in Group 2, it was 73/27, respectively. The average age of patients was 55.09 ± 11.43 years in Group 1 and 55.09 ± 10.41 years in Group 2. The average BMI of patients in Group 1 and Group 2 was 33.69 ± 6.56 kg/m<sup>2</sup> and 33.65 ± 6.50 kg/m<sup>2</sup>, respectively. The average AHI (events/hour) in Group 1 was 58.32 ± 28.33 and Group 2 was 59.09 ± 27.92. The average minimum oxygen saturation in Group 1 was 75.27 ± 50.24, similarly in Group 2, it was 74.95 ± 51.02. The average CPAP titrated pressure was 11.13 ± 1.83 and 10.99 ± 1.78, respectively.

The complete baseline and polysomnographic data are mentioned in Table 1.

In group 1, the Pearson correlation test was used to evaluate the association of demographic and polysomnographic data with titrated CPAP level. It was found that the AHI ( $r = 0.595$ ,  $P < 0.001$ ), minimal SpO<sub>2</sub> ( $r = -0.502$ ,  $P < 0.001$ ), BMI ( $r = 0.494$ ,  $P < 0.001$ ) significantly correlated with optimal CPAP level. The correlation coefficients of other variables are mentioned in Table 2.

Of the anthropometric and polysomnographic variables, stepwise multiple linear regression analysis identified BMI, AHI, and lowest oxygen saturation as independent predictive variables associated with the optimal pressure level. The best predictive equation by stepwise regression analysis was: Optimal CPAP level (cm H<sub>2</sub>O) = 8.401 + (0.053 × BMI) + (0.020 × AHI) – (0.031 × lowest oxygen). Twenty-six percent of the variance in the optimal CPAP level was explained by this equation ( $R^2 = 0.26$ ,  $P < 0.001$ ) [Table 3].

Next, we compared the pressure predicted by our formula and the pressure predicted by manual titration in Group 2. The results calculated by Pearson correlation indicate that pressure predicted by our formula was positively correlated with the titrated pressure [Figure 1,  $r = 0.68$ ,  $P = 0.001$ ].

Our formula provided an optimal estimation of CPAP pressure for 86% of subjects. The rate of underestimation was seen in 9% of subjects and that of overestimation was seen in 5% of subjects.

## DISCUSSION

We had examined 250 OSA subjects who had undergone CPAP titration, developed a new CPAP pressure prediction

**Table 1: Polysomnography data**

Parameter	Group 1	Group 2
Male/female (n)	109/41	73/27
Age (years)	55.09±11.43	55.09±10.41
BMI	33.69±6.56	33.65±6.50
Sleep latency (min)	20.69±24.30	21.60±24.50
Sleep efficiency (%)	79.91±12.50	80.10 ±11.50
Sleep state (%)		
N1	7.86±6.75	7.40±6.42
N2	72.87 ±12.96	72.50±13.03
N3	14.26±11.32	14.00±11.36
REM	5.30±5.84	5.41±5.90
Total sleep time, (min)	179.83±57.53	180.12±56.53
AHI (events/h)	58.32±28.33	59.09±27.92
Minimum oxygen saturation (%)	75.27±50.24	74.95±51.02
CPAP titrated pressure (cm H <sub>2</sub> O)	11.13±1.83	10.99±1.78

BMI: Body mass index, REM: Rapid eye movement, CPAP: Continuous positive airway pressure, AHI: Apnea-hypopnea index

**Table 2: Correlating optimum pressure level with the demographic and polysomnographic data**

Variable	Co-relation coefficient	P
Age	-0.08	0.31
BMI	0.494	0.001
Sleep latency (min)	0.03	0.45
Sleep efficiency (%)	0.01	0.51
Sleep state (%)		
N1	0.36	0.42
N2	-0.29	0.67
N3	-0.01	0.72
REM	0.04	0.31
Total sleep time (min)	0.17	0.20
AHI (events/h)	0.90	0.001
Minimum oxygen saturation (%)	0.50	0.001

Values are mean±SD unless otherwise indicated. BMI: Body mass index, REM: Rapid eye movement, AHI: Apnea-hypopnea index, RDI: Respiratory disturbance index, SD: Standard deviation

**Table 3: Parameters noted after multiple linear regression analysis**

Model	B	Significant
Constant	8.401	0.000
BMI	0.053	0.001
AHI	0.020	0.001
Oxygen saturation	-0.031	0.000

AHI: Apnea-hypopnea index, BMI: Body mass index

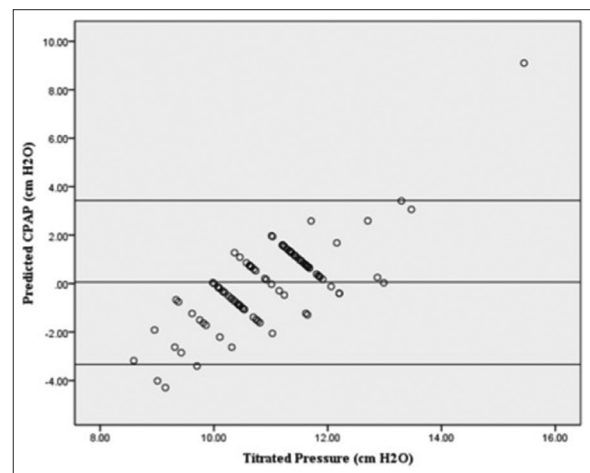
equation for Indian patients and then compared with the pressure calculated by manual titration.

In this study, the average age of the patients was 55.09 ± 11.43. It is comparable to the other studies done by Schiza *et al.*,<sup>[6]</sup> 54.6 ± 10.67. In studies done among Asian countries where Wu *et al.*, from Taiwan<sup>[7]</sup> and Akahoshi *et al.* from Japan,<sup>[8]</sup> the average age was 53.3 ± 13.1 and 52.9 ± 12.4, respectively.

The average BMI of patients in our study was 33.69 ± 6.56 kg/m<sup>2</sup>. In studies done in non-Asian countries by Stradling *et al.*, in Britain, average BMI was<sup>[9]</sup> 36.5 ± 6.5 kg/m<sup>2</sup>. In a study done in Canada by Skomro *et al.*,<sup>[10]</sup> average BMI was 37 ± 8 kg/m<sup>2</sup>. Among Asian countries, Lai *et al.*,<sup>[11]</sup> in a study conducted in Taiwan found that average BMI was 27.1 ± 3.6 and Ito *et al.*,<sup>[12]</sup> in Japan found the average BMI to be 25.1 (21.2, 30.4). It was seen that non-Asians have a higher BMI than Asians. Indians have higher BMI than other Asians.

The average AHI (events/hour) in our study was 58.32 ± 28.33. Loredó *et al.* in a study done in the USA<sup>[13]</sup> found the average AHI to be 55.5 ± 31.3. Similarly, by Basoglu and Tasbakan (2012), in Turkey<sup>[14]</sup> found it to be 56.7 ± 22.8. Among Asian countries, Ito *et al.*,<sup>[12]</sup> found the average AHI to be 33.9 (19.5, 59.9). Chuang *et al.* from Taiwan found it to be<sup>[15]</sup> 58 ± 23.

In our study, it was found that the AHI ( $r = 0.595$ ,  $P < 0.001$ ), minimal SpO<sub>2</sub> ( $r = -0.502$ ,  $P < 0.001$ ), BMI ( $r = 0.494$ ,  $P < 0.001$ ) significantly correlated with optimal CPAP level and these parameters were used for formulating the equation. The best predictive equation by stepwise regression analysis was: Optimal CPAP level (cm H<sub>2</sub>O) = 8.401 + (0.053 × BMI) + (0.020 × AHI) - (0.031 × lowest oxygen). On a similar basis, a study done by Wu *et al.*, in Taiwan, the equation was 6.380 + 0.033 × AHI - 0.068 × SaO<sub>2</sub> + 0.171 × BMI.<sup>[7]</sup>



**Figure 1:** Correlation of predicted continuous positive airway pressure from our formula with titrated pressure. The upper and lower lines indicate 95% confidence intervals

In other studies, similar parameters were used during the multiple linear regressions analyses. BMI was seen as the most common variable in the mathematical equations, where eighteen studies had included it. In our study, the coefficient was 0.053. The meta-analysis done by Camacho *et al.* showed that the coefficient mean value for BMI ranges between 0.02 and 0.205. In the Asian studies, the mean value for the coefficient was 0.16871, whereas, in the non-Asian studies, the mean value for the coefficient was 0.1003, demonstrating that this variable emerged as a more heavily weighted variable than other variables during the multiple linear regressions analyses. Given that for the Asian studies, the means for BMI were between 25.1 kg/m<sup>2</sup> and 28.4 kg/m<sup>2</sup>. While in the nonAsian studies, the means for BMI were between 30.9 kg/m<sup>2</sup> and 40.6 kg/m<sup>2</sup>.<sup>[2]</sup>

AHI was a variable in mathematical equations for 17 studies (meta-analysis). In our study, the coefficient for AHI was 0.020. The coefficient for AHI ranged between 0.01 and 0.18 and for RDI ranged between 0.01301 and 0.041. The overall mean coefficient for AHI was 0.0442 for all studies and 0.03963 for Asian and 0.04878 for non-Asian studies.<sup>[2]</sup>

For the five studies that included ODI, four studies that evaluated mean oxygen saturation, and the four studies that evaluated the lowest oxygen saturation, the factor that had the largest influence when used was the mean oxygen saturation. The mean coefficient value for mean oxygen saturation was 0.19525, compared to 0.04417 for ODI and 0.065 for lowest oxygen saturation.<sup>[16]</sup> In this study, the coefficient for the lowest oxygen saturation was 0.031.

We compared the pressure predicted by our formula and the pressure predicted by manual titration in Group 2. The results calculated by Pearson correlation indicate that pressure predicted by our formula was positively correlated with the titrated pressure [Figure 1,  $r = 0.68$ ,  $P = 0.001$ ]. Similarly, in the study done by El Solh *et al.*,<sup>[16]</sup> the correlation coefficients between the titration study and predicted pressure were 0.86. In the study done by Luo *et al.*<sup>[17]</sup>  $R = 0.677$ ,  $R^2 = 0.459$ ; calculated pressure  $7.7 \pm 1.4$  cwp (centimeters of water pressure) versus  $7.3 \pm 1.5$  cwp. CPAP titration was compared to APAP, and APAP pressure was higher.

Although the mathematical equations have helped improve PAP titration study success, the formulae are not completely generalizable secondary to physical, behavioral, comorbidity, and PSG differences in OSA patients. More studies evaluating the utility of mathematical equations for prescribing CPAP for home use are needed.

## CONCLUSION

The equation was developed, which will help in estimating CPAP pressure. As this is a single-center analysis, this equation should be tested for accuracy with other set of the population from the hospital setting. Furthermore, the other centers in India can formulate the formula as per their patient

population for more generalization. The results suggest that manual titration pressure correlates with the pressure derived from the predictive equation in our study. The shortcomings of the study are parameters such as NC, smoking, and alcoholic status could not be added in the equation, and further advancements can be done in this regard.

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Nil.

## Conflicts of interest

There are no conflicts of interest.

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